FOOD AND DRUGS AUTHORITY

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FDA RELIANCE GUIDELINE ON REGULATORY DECISION-MAKING

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Date of Revision	Version Number	Changes made and/or reasons for revision
2nd January 2019	01	Initial issue
1st March 2023	02	General review in line with the current structure and amendment of policy to a guideline.

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Executive Summary

This guideline is intended to assist applicants appreciate the FDA's regulatory reliance pathway which seeks to bring greater efficiency to the regulatory process by eliminating duplicative work, strengthening regulatory systems, promoting harmonization and optimizing resource utilization with a focus on value-added activities without sacrificing product quality, safety, or efficacy.

1.0 Introduction

To promote a more efficient approach to regulation, thereby improving access to quality-assured, effective and safe medical products, the FDA has developed and implemented alternative /non-routine authorization application pathways to the standard/routine approval pathways, especially for applications where the safety and efficacy of the product have already been confirmed or when the Clinical Trial has been approved and/or initiated (partly or wholly – phase I/II/III) in a well – resourced setting and by well-resourced National Regulatory Authorities (NRAs).

The instituted alternative pathways are designed to facilitate regulatory reviews and evaluations in a timely manner and at the same time, accelerate the evaluation process without compromising the quality of work conducted on submitted documents while ensuring that authorized products or clinical trials meet established and published regulatory requirements, which are internationally accepted. Further, it focuses on risk-based evaluations, concentrating on what is locally critical (*i.e.* value-added in terms of resource/time investment) versus what can be leveraged/relied upon from decisions made by a well-resourced NRAs that operates within the ICH region and other reference countries, Regional Economic Communities (RECs).

The aim is to expedite the entire application submission and evaluation process towards timely regulatory decision-making. The activity is achieved in a variety of ways, including information and/or work-sharing and reliance (partly or fully) on assessment reports generated by well-resourced NRAs, GMP/GCP inspection reports, QC laboratory reports and similar documents.

The FDA's perception of reliance implies that the work done is shared by the well-resourced NRA (e.g. through assessment reports, inspection reports, QC lab reports, etc...), while the FDA uses this work according to its own scientific knowledge and regulatory procedures (such as differences in conditions of use, patient population,

etc...) and retains its own regulatory responsibilities. The FDA accepts that reliance can be unilateral, bilateral (mutual) or multilateral and it will leverage the information in the imported reports and/or decisions to arrive at a regulatory decision but will maintain its own regulatory responsibilities for decision-making.

Note: The FDA shall activate the reliance pathway to facilitate regulatory decisions either on a case-by-case basis or at the explicit request of the Applicant.

The objective of this guideline is to expedite the evaluation and decision-making process of applications submitted, which have been approved by a well-resourced NRA while retaining the FDA's regulatory responsibilities and decision-making. The FDA will consider and give significant weight to assessment reports prepared by a well-resourced NRA or trusted institution or REC or to any other authoritative information in reaching its own decision. This guideline will provide high level requirements spanning the full life cycle of a medical product.

1.1 Legal Basis

Section 148 Public Health Act, 2012, Act 851 gives the Food and Drugs Authority the mandate to issue guidelines and codes of practice in connection with the regulation of food and drugs and any other products or devices regulated by the Authority.

1.2 Scope

This guideline shall be applicable to marketing authorization of human and veterinary allopathic drugs, vaccines and other biological products and medical devices, authorization of all phases of Clinical Trials, Good Manufacturing Practice inspection, Quality Control testing, vigilance, lot release, market surveillance and control and licensing establishment.

2.0 DEFINITIONS AND ABBREVIATIONS

2.1 DEFINITION OF TERMS

Well-resourced or reference National Regulatory Authority or Entity

A well-resourced or reference national regulatory authority is:

I. a member of ICH prior to 23 October 2015, namely: the US Food and Drug Administration, the European Commission and the Ministry of Health, Labour and Welfare of Japan also represented by the Pharmaceuticals and Medical Devices Agency; or

II. an ICH observer prior to 23 October 2015, namely: the European Free Trade Association, as represented by Swissmedic and Health Canada; or

III. a regulatory authority associated with an ICH member through a legally binding, mutual recognition agreement prior to 23 October 2015, namely: Australia, Iceland, Liechtenstein, and Norway.

IV. ICH regulatory member such as HAS, Singapore; MHRA United Kingdom; MFDS, Republic of Korea.

V. A regulatory authority designated by the WHO through the WHO GBT as a Maturity Level 3 or 4 NRA or a WHO Listed Authority.

VI. An entity formed by a regional body or global body dedicated to expanding universal health coverage, as well as directing and coordinating the regional or global response to health issues and/or emergencies and promoting healthier lives (e.g., WAHO, WHO, etc.)

2.2 ABBREVIATIONS

AMA	African Medicines Agency
AVAREF	African Vaccine Regulatory Forum
API	Active Pharmaceutical Ingredient
CT	Clinical Trials
EC	European Commission
EMA	European Medicines Agency
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
HPTD	Health Products and Technologies Division
ICH	International Council on Harmonization
ILAC	International Laboratory Accreditation
MHLW	Ministry of Health, Labour and Welfare Japan
MAH	Marketing Authorization Holder
NRA	National Regulatory Agency
PAR	Public Assessment Report
PMDA	Pharmaceutical and Medical Devices Agency
PQ	Prequalification
QC	Quality Control
TGA	Therapeutic Goods Administration
US FDA	United States Food and Drug Administration
WHO	World Health Organization

3.0 Requirements

3.1 Tool for implementation

The following tools shall be used to ensure full implementation and compliance to the reliance route:

3.1.1 Clinical Trials Authorization

1. If the product under investigation has already been evaluated and listed as a WHO

Prequalified Product through the WHO PQ collaborative registration procedure between WHO and NRAs

2. If the product under investigation has already been evaluated and listed as a product of either the WHO collaborative registration pilot for stringently authorized products, including through the EU's Article 58 Procedure or the Swiss medic's Marketing Authorization for Global Health products or the International Generic Drug Regulatory Program (launched July 2014).
3. If either the trial or the investigational product has been authorized or granted marketing authorization in either an ICH founding regulatory member state or region (such as EC (EMA), United States (United States Food and Drugs Administration), Japan (MHLW/PMDA) or an ICH standing regulatory member state or region (such as Canada (Health Canada), Switzerland (Swissmedic). Further, products registered by TGA of Australia, Iceland, Liechtenstein, MHRA of UK and Norway shall be considered through the reliance route.
4. If the product under investigation has already been evaluated and approved for use by a WHO GBT Maturity Level 3 or 4 NRA or a WHO Listed Authority (WLA).
5. If either the trial or the investigational product has been evaluated and judged satisfactory at a joint review meeting facilitated by the World Health Organization under the African Vaccine Regulatory Forum (AVAREF).

3.1.2 Registration and/or Marketing Authorization

1. The product should have been evaluated and listed as a WHO Prequalified product through the WHO PQ collaborative registration procedure between WHO and NRAs

2. The product has already been evaluated and granted MA for use by a WHO GBT Maturity Level 3 or 4 NRA or a WHO Listed Authority.

3. The product should have been evaluated and listed as a product of either the WHO collaborative registration pilot for stringently authorized products, including through the EU's Article 58 Procedure or the Swissmedic's Marketing Authorization for

Global Health products or the International Generic Drug Regulatory Programme (launched July 2014). The product should have been registered and/or granted marketing authorization in either an ICH founding regulatory member state or region (such as EC (EMA), United States (United States Food and Drugs Administration), Japan (MHLW/PMDA) or an ICH standing regulatory member state or region (such as Canada (Health Canada), Switzerland (Swissmedic). Further, products registered by TGA of Australia, Iceland, Liechtenstein, MHRA of UK and Norway shall be considered through the reliance route.

4. The product should have been evaluated and listed as an output of the West African Medicines Harmonization initiative of the Economic Community of West African States (ECOWAS).

3.1.3 Regulatory Inspections

2. The product should have been evaluated and listed as a WHO Prequalified Product through the WHO PQ collaborative registration procedure between WHO and NRAs, and the manufacturing facility should have been inspected by the NRA in the country of origin and the WHO pre-qualification team.

3. The manufacturing facility of the product of interest should have been inspected by an NRA designated by the WHO via WHO GBT as a Maturity Level 3 or 4 NRA or as a WHO listed Authority.

4. The product should have been evaluated and listed as a product of either the WHO collaborative registration pilot for stringently authorized products, including through the EU's Article 58 Procedure or the Swissmedic's Marketing Authorization for Global Health products or the International Generic Drug Regulatory Programme (launched July 2014), and the manufacturing facility should have been inspected by the NRA in the country of origin and/or the WHO pre-qualification team.

5. The product should have been registered and/or granted marketing authorization in either an ICH founding regulatory member state or region (such as EU (EMA), United States (United States Food and Drugs Administration), Japan

(MHLW/PMDA) or an ICH standing regulatory member state or region (such as Canada (Health Canada), Switzerland (Swissmedic). Further, a product registered by TGA of Australia, Iceland, Liechtenstein, MHRA of UK and Norway shall be considered through the reliance pathway. The manufacturing facilities within which the products are manufactured should have been inspected for cGMP compliance with by the country of origin with a satisfactory inspection outcome.

6. The product should have been evaluated and listed as an output of the West African Medicines Harmonization (WAMH) initiative of the Economic Community of West African States (ECOWAS), or a similar entity and the manufacturing facility inspected by WAMH or a similar entity.

7. Further information on eligibility can be obtained from the document with the following link:
http://www.fdaghana.gov.gh/img/organisation/WAIVER%20REQUIREMENTS%20FOR%20cGMP%20INSPECTIONS-.pdf

3.1.4 Vigilance

The FDA continually ensures the safety of marketed products through its established pharmacovigilance system. To ensure that safety issues are promptly identified, and the necessary interventions implemented, the FDA considers decisions from WHO Listed Authorities on the safety of medical products that impact negatively on the health of patients. The regulatory decisions by the FDA – leveraging safety decisions from well-resourced or reference NRAs - are geared towards ensuring appropriate and safe use of registered medical products.

1. The medical product of concern should have been registered and/or granted marketing authorization in either an ICH founding regulatory member state or region, such as EC (EMA), United States (United States Food and Drugs Administration), Japan (MHLW/PMDA) or an ICH standing regulatory member state or region (such as Canada (Health Canada), Switzerland (Swissmedic). Further, products registered by TGA of Australia, Iceland, Liechtenstein, MHRA of UK and Norway, as well as those authorized through the EU's Article 58 Procedure, or the

Swissmedic's Marketing Authorization for Global Health products shall be considered through the reliance route.

3.1.5 Laboratory Testing (Quality Control)

On a case-by-case basis, the Center for Laboratory Services and Research (CLSR) leverage a provision in the Public Health Act 2012, Act 851, section 127 (5) that allows the FDA to rely on or recognize analytical reports from laboratories which are WHO Pre-qualified or ISO/IEC 17025:2017 accredited and awarded by an ILAC member.

4.0 Alternative /Non-Routine Application Approval Pathways

Reliance pathways to Facilitate Regulatory Decisions

Authorization pathways used by the FDA wherein its decisions regarding the authorization of a clinical trial or marketing authorization of medical product could be accelerated by the reliance on prior assessment report prepared by a well-resourced regulatory authority, mostly operating within the ICH region or agencies or programmes affiliated to the WHO (e.g., AVAREF, PQ, etc,), NRAs designated by the WHO via the WHO GBT tool as ML3, ML4 or WLA and other reference NRAs (such as MHRA of UK, Norway, etc) or bodies such as the RECs. The FDA shall remain responsible and accountable for all regulatory decisions taken, and guided by the benefit-risk assessment which focuses on the intended local population and indication(s).

5.0 Reliance Procedure

5.1 Verification

The FDA shall 'verify' that the product intended to be imported and distributed in Ghana or the Clinical trial to be conducted in Ghana has been duly registered or authorized or given a positive opinion by a well-resourced NRA or by a reference

body.

In the case of MA, the product should have been granted marketing authorization, and the product characteristics (use, dosage, precautions) for local MA should conform to that agreed in the authorization by the well-resourced or the reference body. In addition, there should be an assurance that the product is either identical to or similar to that approved by the well-resourced or the reference body in terms of quality, safety and efficacy.

For Clinical trial submissions, the application (protocol, IB, nonclinical reports, previous study reports and other relevant documents) should be identical to that submitted, evaluated and approved by the well-resourced or reference body.

Notwithstanding, the FDA reserves the right to subject all submissions for approval to an 'abridged' evaluation of a certain part of the application (e.g. relevant to use under local condition) such as product quality data in relation to climatic conditions and distribution infrastructure and a benefit-risk assessment in relation to use in the local ethnic population, medical practice/culture and patterns of disease and nutrition. Typically, the verification pathway shall take sixty thirty (60) working days (excluding clock stops) as opposed to the 120 working days in the case of medicines, vaccines and biological product registration, and 60 working days in the case of Clinical Trial Authorization for the routine pathway.

5.2 Other Acceptable Reliance Mechanisms

- Regional reliance: This means that the FDA shall rely on the regulatory position/ opinion resulting from a centralized evaluation of an application (MA, CT, etc) or other regulatory submissions. The regulatory position/opinion should have been prepared or generated by a platform of competent and trusted agencies and /or corporation/collaboration with other regulators from a well-resourced NRA. Nonetheless, the FDA shall have the independent final decision to apply the

regulatory position/opinion.

- Unilateral or mutual recognition: this means that the FDA shall recognize regulatory position/opinion from a well-resourced NRA or listed reference bodies leveraging treaties or equivalent, which will provide maximal benefit to the FDA with regards to expeditious decision-making and expended work towards decision-making.

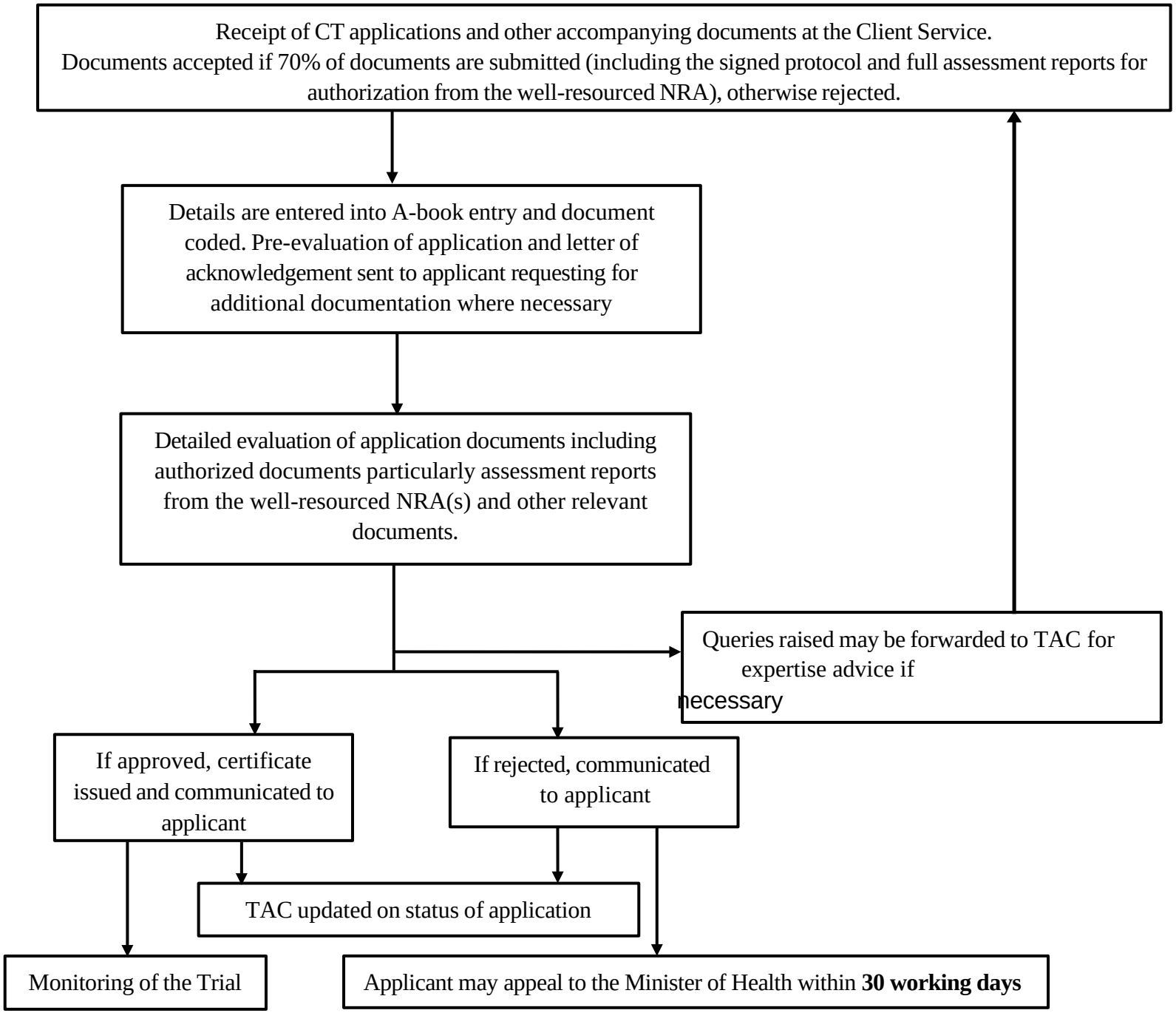
5.3 Documentation

In addition to the full assessment report from the well-resourced or the reference NRA and/or public assessment report (to be decided by the FDA-on a case-by-case basis), the applicant shall be required to submit a full product development dossier - (CTD Modules I-VI in the case of MA) (as required by the relevant FDA's guidelines) or Study Protocol, Investigational Brochure (IB), ethics approval, insurance of the study and information on the development/manufacture of the product (e.g., IMPD for unregistered medicine or vaccines, SmPC/PIL for registered product) - to support the decision-making process by the FDA, if the reliance pathway is applied. Specific guidelines for each of the functionalities are available on the FDA's website.

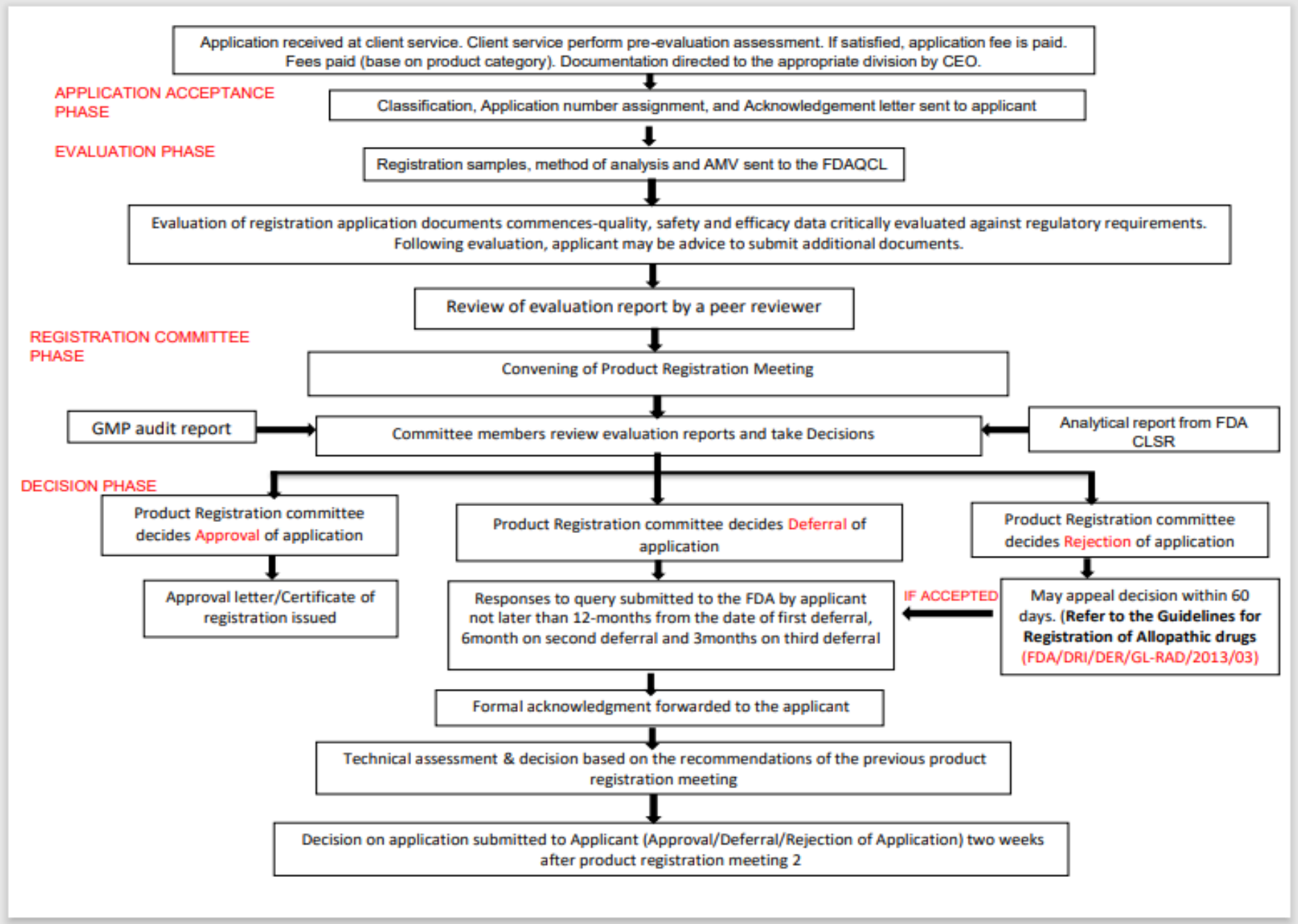
5.4 Evaluation

Evaluation of the imported assessment report(s) shall be executed in accordance with laid down procedures to ensure the appropriateness and completeness of the conclusions contained in the report.

6.0 CLINICAL TRIALS AUTHORIZATION



7.0 MARKETING AUTHORIZATION PATHWAY



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16. Guidelines for Registration of UK Generics. GUIDELINES FOR REGISTRATION OF UK GENERICS.pdf (fdaghana.gov.gh)

17. List of WHO-Listed Authorities (WLA) (in alphabetical order) as of May 2024. list_of_wla_may24.pdf (who.int)

18. List of National Regulatory Authorities (NRAs) operating at maturity level 3 (ML3)[1] and maturity level 4 (ML4)[2] (as benchmarked against WHO Global Benchmarking Tool (GBT) (in alphabetical order) – As of June 2024 List of National Regulatory Authorities (NRAs) operating at maturity level 3 (ML3) and maturity level 4 (ML4) (who.int).

19. ICH Member & Observer -Current Member & Observer - https://www.ich.org/page/members-observer